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Diagnosis and management of oral allergy syndrome (pollen-food allergy syndrome)

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INTRODUCTION — The oral allergy syndrome (OAS) describes allergic reactions that occur upon ingestion of certain fresh fruits, nuts, vegetables, or spices in pollen-sensitized individuals. The symptoms result from contact urticaria of the mucosal surface that contacts the food. Symptoms are usually limited to the mouth and throat and observed with raw forms of the food, because the responsible allergens are rapidly inactivated by digestion and cooking, although this is not uniformly true. Systemic reactions are observed in 2 to 10 percent of patients, and reactions to cooked plant foods (including roasted nuts) are possible.

In this topic review, the term OAS is used to describe reactions limited to the oropharynx. Pollen-food allergy syndrome (PFAS) is a broader term that encompasses both oropharyngeal and systemic symptoms and is the preferred term for the spectrum of reactions caused by allergens in plant foods that are homologous to pollen allergens.

This topic review presents the evaluation, diagnosis, and management of patients with PFAS. The clinical manifestations and pathogenesis of PFS are reviewed separately. (See "[Clinical manifestations of oral allergy syndrome \(pollen-food allergy syndrome\)](#)" and "[Pathogenesis of oral allergy syndrome \(pollen-food allergy syndrome\)](#)".)

DIAGNOSIS — There are no established diagnostic criteria for the diagnosis of PFAS; however, the following components should be present:

- A history of symptoms consistent with PFAS
- Evidence of allergic sensitization to the plant food in question

- Evidence of allergic sensitization to pollen
- A known correlation between the plant food(s) in question and a pollen(s) to which the patient is sensitized ([figure 1](#))

EVALUATION — As with any form of food allergy, the evaluation of PFAS combines a carefully gathered history, physical examination, objective testing for specific IgE to food and/or pollen, and possible oral food challenge [[1](#)]. All of these components are not necessary in each case, and the extent of the evaluation, as well as the approach to management, is influenced by the food to which the patient reacted and the severity of the symptoms.

Most diagnostic allergy procedures, especially skin testing and food challenges, should be performed by allergy specialists with training in the management of serious allergic reactions. In vitro tests for specific IgE may be performed by the non-specialist, although definitive interpretation may require a specialist's input.

History — Important information obtained from the history includes the following:

- Has the patient experienced oropharyngeal symptoms, systemic symptoms, or both? Patients with systemic symptoms should be thoroughly evaluated by an allergy specialist and provided with epinephrine autoinjectors. (See '[Management](#)' below.)
- Are symptoms of pollen allergy present? In many cases, pollen allergy (pollinosis) can be detected clinically as rhinitis, conjunctivitis, or asthma symptoms, which occur in a seasonal pattern ([figure 2](#)). If the patient does not have obvious symptoms of pollinosis, then testing for pollen sensitization should be performed.
- Has the patient reacted to other plant foods related to the one in question? Patients may not recall reactions to foods they uncommonly eat unless specifically asked.
- Are cooked forms of the food tolerated? The development of symptoms with raw foods but not with the cooked forms is very suggestive of PFAS.

Objective testing for food allergy — Our approach to most patients with suspected PFAS is to test in parallel with both commercial extracts (when available) and prick-by-prick testing to fresh foods, except in the situations mentioned below. (See '[IgE immunoassays](#)' below.)

Prick-by-prick skin testing with fresh foods — The preferred method of testing in most cases is skin prick testing (SPT) with fresh fruits and vegetables using the prick-by-prick technique. Prick-by-prick testing is performed by inserting

the test device into the fruit, withdrawing, and then immediately pricking the patient's cleaned skin. It is important to prick all edible parts of the food (eg, both the outer skin and the flesh of fruits) with the testing device in order to recreate the allergen exposure that would result from eating these foods. (See ["Diagnostic tools for food allergy"](#).)

For most foods implicated in PFAS, the prick-by-prick method appears to be more sensitive than SPT with commercial extracts [2,3]. In one study, the sensitivity of SPT using a commercial extract of apple was 2 percent, compared to 82 percent when prick-by-prick technique was used with fresh apple [2]. The prick-by-prick technique also proved to be the more sensitive for carrot, celery, cherry, tomato, orange, and peach, although the difference was not as dramatic. Each of these plant foods contains unstable allergens.

In contrast, allergy to foods containing stable allergens, such as peanut, hazelnut, and pea, may be best detected with commercial extracts [2].

Commercial food extracts — Skin testing with commercial extracts may be most useful in the following settings:

- To evaluate for sensitization to tree nuts and legumes, such as peanut, hazelnut, and pea, which contain stable allergens [2]. Commercial extracts may be inadvertently enriched for stable allergens as a result of processing.
- To evaluate for sensitization to foods that might be difficult to prepare or irritating to the skin, such as spices.
- To help assess the risk of systemic reactions: individuals with positive skin tests to commercial Rosaceae food extracts were more likely to experience systemic reactions than those with positive skin tests only to fresh extracts (64 percent versus 6 percent) [4]. As mentioned previously, commercial extracts may be enriched for the stable allergens, which are associated with systemic reactions. (See ["Pathogenesis of oral allergy syndrome \(pollen-food allergy syndrome\)"](#).)

IgE immunoassays — There are clinical situations in which the most appropriate initial test for food-specific IgE is an in vitro immunoassay. Examples include patients with a history of life-threatening anaphylaxis to a small amount of the implicated food, those with dermographism or extensive skin disease, those who cannot discontinue interfering medications, and those with unstable asthma. These issues are presented in more detail separately. (See ["Diagnostic tools for food allergy"](#).)

Diagnostic pitfalls — Both skin testing and in vitro testing in the diagnosis of PFAS are complicated by the variable and unstable nature of the responsible

allergens and the extensive cross-reactivity among them. Both false negative and false positive results are common in patients with PFAS. As in all forms of IgE-mediated food allergy, testing must be interpreted in the context of a careful clinical history.

Clinicians should be mindful of the following issues when performing evaluations for PFAS:

- Unstable food allergens are often destroyed during the production of commercial extracts, and thus testing with these extracts often has low sensitivity for detecting sensitization to the allergens that are typically responsible for PFAS [5].
- IgE immunoassays for IgE specific to various foods (which were previously called RAST tests) have not been systematically evaluated in the diagnosis of PFAS. The use of fresh food to coat the immunoassay disk has been utilized in some reports; however, this is impractical outside of research centers [6,7].
- Testing with fresh fruits and vegetables is sometimes confounded by natural variations in allergen levels due to differences among the various varieties (eg, cultivars), ripeness, or changes induced by storage.
- Positive tests may result from the presence of cross-reactive panallergens in fruits and vegetables from the same family, as well as in plant foods and the related pollens [8]. However, these may not be the allergens responsible for the patient's symptoms. (See "[Pathogenesis of oral allergy syndrome \(pollen-food allergy syndrome\)](#)".)

Objective testing for pollen sensitization — Confirmation of pollen sensitization either by skin testing (most accurate) or by IgE immunoassays is necessary to make a conclusive diagnosis of PFAS. In reality, patients sometimes clearly describe symptoms of respiratory allergy during a specific pollen season, allowing for a reasonably certain diagnosis based solely on this history ([figure 2](#)). It may not be necessary to prove pollen sensitization if the patient's culprit food and seasonal symptoms match (ie, reactions to apple in a patient with rhinitis during tree pollen season) and if past reactions were consistently mild and limited to the oropharynx.

However, pollen sensitization should be confirmed by testing if either of the following is true:

- If it is unclear from the history that the patient has pollen allergy.
- If the patient has experienced systemic symptoms, because patients without pollen sensitization may have an isolated allergy to a plant food (unrelated to

pollen) and be at higher risk for systemic reactions.

Skin testing — Skin testing is the best method of demonstrating pollen sensitization. The performance and interpretation of skin testing for environmental allergies is reviewed separately. (See ["Overview of skin testing for allergic disease"](#).)

Immunoassays — If skin testing is not available or not possible because the patient is taking interfering medications or for other reasons, then IgE immunoassays may be helpful in detecting sensitization to pollens. These are generally less sensitive than skin tests. (See ["Overview of skin testing for allergic disease"](#).)

Oral food challenges — Patients with PFAS will frequently have positive skin or in vitro tests to several related foods within a plant family, as mentioned above. However, as in other forms of IgE-mediated food allergy, positive tests do not necessarily predict clinical symptoms upon ingestion. Thus, oral food challenge remains the only definitive method of identifying clinical reactions.

Although oral food challenges are the most conclusive means of confirming food allergy, challenges in PFAS may be impacted by some of the same issues that affect skin testing. Allergen levels can vary among cultivars, within different parts of the fruit (peel versus flesh), with ripeness, or due to changes induced by storage [9]. Challenge studies suggest that a history of clinical reactivity can be confirmed by oral food challenges in only one-third of melon allergic patients, in two-thirds of patients allergic to fruits from Rosaceae family (peach, plum, pear, apple, almond, apricot, and strawberry), and in approximately 80 percent of patients allergic to fruits from Prunoideae family (peach, apricot, plum, and cherry) [8,10,11].

The importance of obtaining a definitive diagnosis depends upon the severity of the reaction, nutritional needs, food preferences, and social issues. In many cases, diet is empirically limited based on the clinical history and the results of SPTs, rather than formal food challenges. However, food challenge may be indicated in certain situations:

- In patients with past systemic reactions to mixed foods, when the culprit food could not be unequivocally identified through skin or in vitro testing. In this case, the challenge would be performed in order to ascertain that the responsible food had been correctly identified.
- In patients reporting symptoms to a specific food, in whom testing failed to demonstrate sensitization to that food. Challenge would be done in this situation because testing may have been falsely negative due to allergen variability. (See ["Objective testing for food allergy"](#) above.)

- In patients in whom it is unclear if cooking or other processing eliminates the symptoms. Challenge can be performed with raw and cooked forms of the food.
- In patients with past systemic reactions to one food who have not been previously exposed to the related foods (eg, systemic reactions to hazelnut in a patient who hasn't eaten other tree nuts, or systemic reactions to peach in a patient who hasn't eaten other Rosaceae fruits).

In deciding on the challenge procedure (office versus hospital setting, intravenous access, the rate and quantity of administered food), risks should be assessed based on the severity of previous reactions, food involved, and test results. An open challenge with the food in its natural form should always follow a negative blinded challenge. (See "[Diagnostic tools for food allergy](#)".)

Special care is needed in preparing food for blinded challenges to confirm PFAS because freeze-drying, heating, and other processing methods can destroy the fragile allergens, leading to false negative results [[10](#)]. Standardized protocols for challenges to raw fruits and vegetables are not available, although research protocols for double-blind, placebo-controlled food challenges to fresh apple, peach, celery, carrot, and melon have been published [[8,10,12-16](#)].

DIFFERENTIAL DIAGNOSIS — Most of the foods that cause PFAS can also cause food allergy without pollen sensitization. Thus, the primary condition that must be differentiated from PFAS is an isolated allergy to the food in question. Any patient who does not have evidence of sensitization to pollens should be considered to have a primary food allergy and managed accordingly, including avoidance of all forms of the food (raw and cooked) and training in the use of epinephrine autoinjectors.

Other conditions that can mimic PFAS include the following:

- Local irritation of the mouth, tongue, or throat caused by spicy, tart, or gritty foods.
- Contact urticaria — Certain foods, such as tomato sauce, citrus fruit, garlic, and berries, can cause a local contact urticaria of the lips and perioral skin. This condition is more common in children and would be suggested by the absence of pollen sensitization.
- Perioral dermatitis or oral contact dermatitis — Perioral dermatitis presents as small papules, vesicles, and/or tiny pustules with erythema and scaling located around the mouth, nose, or periorbital region. Perioral dermatitis can be caused by cosmetic products, or by contact with mango or cashews in

individuals with a history of contact dermatitis in response to poison ivy [17,18]. Contact dermatitis of the lips involves painful swelling or blistering of the lips, followed by peeling during resolution, which occurs over the course of days. The presence of persistent skin lesions distinguishes these conditions from OAS.

- Gastroesophageal reflux disease (GERD) — Patients with GERD can usually be distinguished clinically by less prominent oral symptoms or objectively, by the absence of sensitization to the food or related pollen in question. (See "[Clinical manifestations and diagnosis of gastroesophageal reflux in adults](#)".)
- Eosinophilic esophagitis (EE) — EE can sometimes present with the sensation of food becoming lodged in the throat and may mimic PFAS and other forms of food allergy. Evaluation of dysphagia is discussed in detail elsewhere. (See "[Evaluation of dysphagia in adults](#)".)

FUTURE DIAGNOSTIC TESTS — Tests using recombinant allergens are being developed, which could determine more precisely the allergens to which a patient is sensitized. In theory, these tests could distinguish individuals sensitized to labile antigens, such as Bet v 1 homologs or profilins, from those sensitized to heat and digestion-resistant antigens, and thus differentiate between PFAS and primary plant food allergy. (See "[Future diagnostic tools for food allergy](#)" and "[Pathogenesis of oral allergy syndrome \(pollen-food allergy syndrome\)](#)".)

Component-resolved diagnostics — Component Resolved Diagnostics (CRD) detects IgE sensitization to the individual allergens (components) in the complex food. This technology represents a new direction in food allergy diagnosis. CRD may be especially helpful in distinguishing between cross-reactive allergens and primary sensitizing allergens, and in defining the risk for systemic and/or severe reactions in patients with plant food allergy. CRD is commercially available in Europe and Japan; it is being evaluated by the FDA in the US. (See "[Future diagnostic tools for food allergy](#)", section on 'Technological advances'.)

When individual allergens are known, they can be purified from natural sources or obtained via recombinant methods [19-21]. These individual allergens may be used for skin testing and for IgE immunoassays [22]. ImmunoCAP ISAC® (Immuno Solid-phase Allergen Chip, Phadia) uses protein microarray chip technology to test a panel of 103 individual components from more than 47 plant and non-plant foods and environmental allergens from about 500 µl blood sample obtained by fingerstick [23]. ISAC yields a tremendous amount of information that further increases the sophistication and complexity of pollen food allergy diagnosis. Accordingly, ISAC requires careful interpretation [22].

CRD results still have to be validated with oral food challenges to establish the

clinical correlation. Nevertheless, CRD may offer superior safety, diagnostic accuracy, sensitivity, and specificity. [24,25] Sensitivity may be particularly enhanced in plant food allergy because relevant allergens are unstable and easily degraded during processing (eg, birch Bet v 1 cross-reactive allergens, such as celery Api g 1, apple Mal d 1, soy Gly m 4, or peanut Ara h 8). In one study, sensitivity of CRD was increased by 20 percent compared with the natural extract based immunoassay in the patients with confirmed celeriac (celery tuber) allergy [26].

Potential applications of CRD include the following:

- CRD could differentiate between sensitization to peanut due to cross-reactivity with Bet v 1 and systemic clinical allergy. Among children selected from a larger birth cohort, peanut allergy symptoms were reported by 87 percent of the children with IgE reactivity to pollen unrelated Ara h 1, 2, or 3, but not to Ara h 8 (n = 46), compared with 17 percent of children with IgE reactivity to Ara h 8, but not to Ara h 1, 2, or 3 (n = 23). Symptoms were more severe in the first group [27].
- In a population based birth cohort, IgE to Ara h 2 was the most important predictor of clinical allergy [28]. In contrast, those sensitized to the stable allergens that don't cross-react with pollen, such as Ara h 1 and Ara h 2 or to nsLTPs are at risk for systemic reactions and anaphylaxis [29-31].
- Likewise, patients with kiwi allergy who are mono-sensitized to actinidin (Api g 1) are more likely to experience more severe, systemic symptoms, compared to patients polysensitized to Api g 8 (Bet v 1 homolog) and Api g 9 (profilin) [32].
- CRD allows for detection of IgE to panallergens, such as profilins as well as cross-reactive carbohydrate determinants (CCDs) that are rarely associated with clinical reactivity.

Basophil activation tests — Basophil activation upon stimulation with allergen through binding to specific IgE on the surface of the cell is associated with expression of CD63. In vitro analysis of CD63 expression on basophils from birch pollen allergic individuals with and without PFAS activated with apple extract and with purified recombinant major allergens from apple (Mal d 1), carrot (Dau c 1), and celery (Api g 1) showed specificity and sensitivity comparable to detection of specific allergen IgE [33]. (See ["Future diagnostic tools for food allergy", section on 'Technological advances'](#) and ["Diagnostic tools for food allergy", section on 'In vitro testing'](#).)

MANAGEMENT — There are currently no established practice guidelines for the

management of PFAS and clinicians vary considerably in their practices [[34-36](#)].

One study specifically addressed the diagnosis and management of PFAS by allergists across the United States, using a questionnaire mailed to 226 randomly-selected specialists [[34](#)]. Responses were returned by 122 allergists and revealed an array of practices. Median estimates of the prevalence of OAS in patients with pollen allergy were 5 percent among children and 8 percent among adults, which is significantly lower than the prevalence reported in published series, suggesting underdiagnosis. Fifty-three percent of allergists recommended complete avoidance of causal foods to all patients, whereas 9 percent did not advocate any restrictions. Three percent always prescribed epinephrine for OAS, 30 percent never did, and 66 percent did so on a case by case basis. (See '[Indications for epinephrine](#)' below.)

The approach presented in this topic review is based upon the author's practice experience.

Food avoidance and patient education — Analogous to other forms of food allergy, dietary avoidance of the offending food(s) is the mainstay of the management. Patients are instructed to avoid the specific raw fruits or vegetables or the nuts (roasted or raw) that have caused symptoms in the past. The purpose of avoidance is the prevention of future reactions; there are no studies reporting the impact of avoidance on the natural history of the condition.

All patients with PFAS should be informed of the following [[24,25](#)]:

- There is a small, but definite risk for systemic reactions, which is estimated to be between 2 and 10 percent of patients with PFAS
- Severe reactions can occur upon the first ingestion of a food with cross-reactive proteins
- Systemic reactions to previously tolerated foods can occur
- The natural history of PFAS is unknown

Specific clinical scenarios — In our practice, further management is dictated primarily by the severity of the patient's reaction. The food that caused the reaction is also considered.

Patients with isolated oropharyngeal reactions — In cases of PFAS with isolated oropharyngeal symptoms, testing for sensitization to and prophylactic avoidance of potentially cross-reactive foods is generally not pursued. The patient may be given a printed list of related foods and advised to avoid the raw forms of any that cause symptoms ([figure 1](#)). Patients should be made aware that dehydrated forms of the food may be used in seasonings and can cause reactions (eg, patients allergic to raw celery may react to celery spice, which is dried and

powdered celery) [12].

We suggest that patients who are able to tolerate fruits and vegetables that have been cooked or otherwise thermally processed (microwaved, pasteurized, or baked) continue to eat these forms of the food. When making this recommendation, however, the clinician must be certain that patients are not experiencing other types of reactions to the plant-foods in question. As an example, adult patients with concomitant OAS and atopic dermatitis can have eczematous reactions to fruits and vegetables, even after cooking:

- In one study, double-blind, placebo-controlled food challenges were performed with cooked apple, carrot, or celery, in patients with atopic dermatitis and birch pollen allergy, who experienced OAS and skin symptoms upon ingestion of the foods in raw form. Cooked versions of the culprit foods did not cause OAS, although they did cause worsening of eczema [37].
- Another study showed that heating and digestion abolished the IgE binding ability of Bet v 1 cross-reactive food allergens in apple, celery, carrot; however, there was no effect on the T cell binding epitopes of those allergens [37,38]. Thus, T-cell mediated mechanisms may have been responsible for the worsening of atopic dermatitis observed in some patients.

Patients with systemic reactions — Patients with PFAS who have experienced systemic reactions to a raw food should avoid raw and dehydrated forms of that food. The decision to also avoid cooked versions of the culprit food is influenced by the severity of the patient's reaction and the patient's recent history of tolerating cooked versions, as well as the preferences of the patient and clinician. This decision is usually made on a case by case basis.

Tolerance to cross-reactive foods should be carefully evaluated in any patient who has experienced systemic symptoms, so that the foods that must be avoided are clearly defined. If a cross-reactive food is being ingested on regular basis without adverse symptoms, it is not necessary to test or restrict that food. In contrast, if the cross-reactive food is not a usual part of the diet, a clinician-supervised oral food challenge may be needed to determine tolerance.

Allergy to peach, peanut, tree nuts, or mustard — These foods are associated with higher rates of systemic reactions. We recommend that all patients with established allergies to these foods, regardless of the severity of past symptoms, learn to use and carry an epinephrine autoinjector. (See "[Pathogenesis of oral allergy syndrome \(pollen-food allergy syndrome\)](#)".)

Advice regarding avoidance for patients who have had very mild oropharyngeal symptoms to one of these foods is another difficult issue, especially if the individual

wishes to continue eating cooked forms of the food that are not currently causing symptoms. We typically explain to the patient that the culprit food is more likely to cause dangerous reactions, compared to other foods, and suggest that they convert to strict avoidance if the symptoms seem to be progressing over time.

INDICATIONS FOR EPINEPHRINE — We advise patients with one or more of the following characteristics to carry epinephrine autoinjectors:

- Systemic symptoms in the past.
- Established allergy (regardless of the severity of past reactions) to peanut, tree nuts, or mustard, as these foods are associated with higher rates of systemic reactions.

It is also our practice to advise patients with any of the following characteristics to carry epinephrine:

- Reactions of any severity to cooked plant foods.
- Reactions to particular foods, if practicing in an area where that food is associated with severe reactions, such as peach or apple in Mediterranean countries [39-41]. The phenomenon of certain foods causing more severe reactions in patients in specific geographical locales is discussed in more detail elsewhere. (See "[Pathogenesis of oral allergy syndrome \(pollen-food allergy syndrome\)](#)".)

For patients with isolated oropharyngeal symptoms in the past and/or positive SPT using a commercial extract, we discuss with the patient or parent the unknown natural history of this condition and the uncertain risk of systemic reactions. If the patient/parent's preference is to have access to epinephrine following that discussion, then we generally supply it. (See '[Food avoidance and patient education](#)' above.)

OTHER MANAGEMENT ISSUES

Caution with anti-ulcer treatments — Anti-ulcer drugs increase gastric pH and may impair digestion of food proteins. There are no published studies directly examining the clinical effect of anti-ulcer therapies on PFAS, although the results of studies of other food allergies are of interest [42-44]:

- In a mouse model, anti-ulcer drugs were reported to predispose to allergic reactions to caviar caused by unstable allergens that would be normally destroyed by digestion [42].
- Following a three month course of anti-ulcer drugs, 5 of 153 patients

developed IgE to hazelnut and 2 developed clinical allergy to hazelnut [43]. In addition, 10 percent of the patients showed a boost of pre-existing IgE antibodies and 15 percent de novo IgE formation toward numerous digestion-labile dietary compounds, like milk, potato, celery, carrots, apple, orange, wheat, and rye flour [44].

These observations suggest that patients with PFAS may be at risk for more severe reactions while being treated with anti-ulcer drugs and should practice more careful food avoidance if these medications are required.

Therapies of uncertain benefit

Antihistamines — In a randomized, placebo controlled clinical trial, patients with birch allergy and hazelnut OAS who received a two week course of the H1-receptor antagonist, astemizole, had significantly reduced symptoms on oral challenge compared with placebo; however symptoms did not resolve completely [45]. This approach raises concerns about masking of progressively worsening symptoms and thus increasing risk for severe reactions. We do not recommend premedicating with antihistamines in order to eat the fruit/vegetable. More studies are required to establish safety and efficacy of antihistamine therapy for PFAS.

Pollen immunotherapy — Randomized clinical trials of birch pollen immunotherapy (IT) in subjects with apple allergy suggest that a subset of birch allergic patients with apple allergy benefits from increased tolerance to raw apple or even complete resolution of symptoms [14,46-49]. In contrast, one trial of sublingual immunotherapy for birch pollen allergy did not show efficacy for alleviating PFAS symptoms [50].

The favorable response to IT is associated with decreased skin prick test to raw apple, but no decrease in serum apple-IgE levels. Following discontinuation of IT, skin test reactivity to apple gradually increased, although about 50 percent of patients who benefited from IT still tolerated raw apple more than two years after discontinuation. One authority has suggested that this approach might work best in adults mono-sensitized to birch tree pollen and not to multiple pollens [51]. We generally do not administer pollen IT solely for the purpose of treating PFAS, although we would consider it if the patient is very troubled by the symptoms and understands that this approach only works in a subset of individuals.

Anti-IgE therapy — Although no information regarding PFAS in patients receiving anti-IgE therapy for allergic rhinitis or asthma has been published to date, it appears to be an attractive potential approach in view of the central role of IgE-reactions in the pathomechanism of PFAS. However, clinical trials are necessary to evaluate the role of anti-IgE therapy for treatment of PFAS.

SUMMARY AND RECOMMENDATIONS — Oral allergy syndrome (OAS) and

pollen-food allergy syndrome (PFAS) are IgE-mediated allergic reactions that occur upon ingestion of certain fresh fruits, nuts, vegetables, or spices in pollen-sensitized individuals. The symptoms result from contact urticaria of the mucosal surface that contacts the food and are caused by allergens in plant foods that are homologous to pollen allergens ([figure 1](#)). Systemic reactions occur in 2 to 10 percent of patients. (See ['Introduction'](#) above.)

Diagnosis and evaluation

- The diagnosis of PFAS requires suggestive symptoms in a patient who has evidence of specific IgE to the food in question, accompanied by a clinical history of pollinosis or demonstrated sensitization to a pollen related to the culprit food. (See ['Diagnosis'](#) above.)
- Evaluation of patients suspected of having PFAS involves history, physical examination, objective testing for specific IgE to food and/or pollen, and possible oral food challenge. Extensive evaluation may not be necessary if symptoms are mild and limited to the oropharynx. In contrast, any patient with systemic symptoms requires a thorough evaluation. (See ['Evaluation'](#) above.)
- To assess for allergy to plant foods, we perform skin prick testing (SPT) with both commercial extracts (when available) and the culprit food in raw form (using the prick-by-prick method), in parallel. Each type of testing has advantages for detecting sensitization to different types of allergens, and comparison of the results of the two methods can provide prognostic information on the risk of systemic reactions. However, both false positives and false negatives are common. (See ['Objective testing for food allergy'](#) above.)
- Confirmation of pollen sensitization either by skin testing (most accurate) or by IgE immunoassays is necessary if it is unclear if the patient has pollen allergy, or if there were any systemic symptoms. Patients without pollen sensitization may have an isolated allergy to a plant food and therefore be at higher risk for systemic reactions. (See ['Objective testing for pollen sensitization'](#) above.)
- Oral food challenge remains the only definitive diagnostic maneuver in some cases. In addition, challenge may be helpful for patients with past systemic symptoms who do not know if they tolerate cooked versions of the food or other closely related foods. (See ['Oral food challenges'](#) above.)
- The differential diagnosis primarily consists of isolated plant food allergy. Other disorders to be considered include local irritation (non-immunologic) of

the oral mucosa, contact urticaria (without pollen allergy), eosinophilic esophagitis, GERD, perioral dermatitis, and contact dermatitis of the lips or mouth. (See '[Differential diagnosis](#)' above.)

Management recommendations — There are currently no established practice guidelines for the management of PFAS. The recommendations presented here reflect the author's practice experience. (See '[Management](#)' above.)

- All patients with PFAS should be informed of the small, but definite risk for systemic reactions and the possibility of reacting to related foods upon first exposure. We also provide patients with a printed list of related foods that might also be expected to cause symptoms. (See '[Food avoidance and patient education](#)' above.)
- Patients who are significantly bothered by PFAS symptoms limited to the oropharynx will want to avoid the raw foods that cause symptoms.
- The long-term consequences of continuing to ingest raw foods that cause PFAS are unknown. For patients who wish to continue eating foods that cause mild symptoms limited to the oropharynx, we suggest not restricting food intake (**Grade 2C**). (See '[Food avoidance and patient education](#)' above and '[Patients with isolated oropharyngeal reactions](#)' above.)
- Patients with PFAS and systemic symptoms must avoid the raw form of the responsible food. We suggest that such patients also avoid cooked forms of the responsible food (**Grade 2C**). Exceptions to this may be patients who have recently tolerated cooked forms of the food, whose systemic symptoms to raw food were not life-threatening, and who strongly desire to continue eating cooked forms. If a patient wishes to continue eating cross-reactive foods, we evaluate for allergy to the foods in question, so that the foods that must be avoided are clearly defined. If the patient wishes to continue eating other foods to which they test positive, but have not eaten recently, then we perform a clinician-supervised oral food challenge to determine tolerance. (See '[Patients with systemic reactions](#)' above.)
- Patients with PFAS who experienced systemic symptoms in the past should carry epinephrine autoinjectors. (See '[Indications for epinephrine](#)' above.)
- We suggest that patients who have not experienced systemic reactions carry epinephrine autoinjectors if any of the following are true (**Grade 2C**):

Allergy to peanut, tree nuts, or mustard has been objectively established

The patient experienced an oropharyngeal reaction to a cooked plant food

The patient had a positive SPT to a commercial extract for the culprit food

The patient reacted to a food that is associated with higher rates of systemic reaction in the geographical area in question (eg, a patient with allergy to apple living in Spain)

(See ['Indications for epinephrine'](#) above.)

- Therapies of unproven benefit for PFAS include prophylactic administration of H1-antihistamines, immunotherapy for pollinosis, and anti-IgE therapy. (See ['Other management issues'](#) above.)

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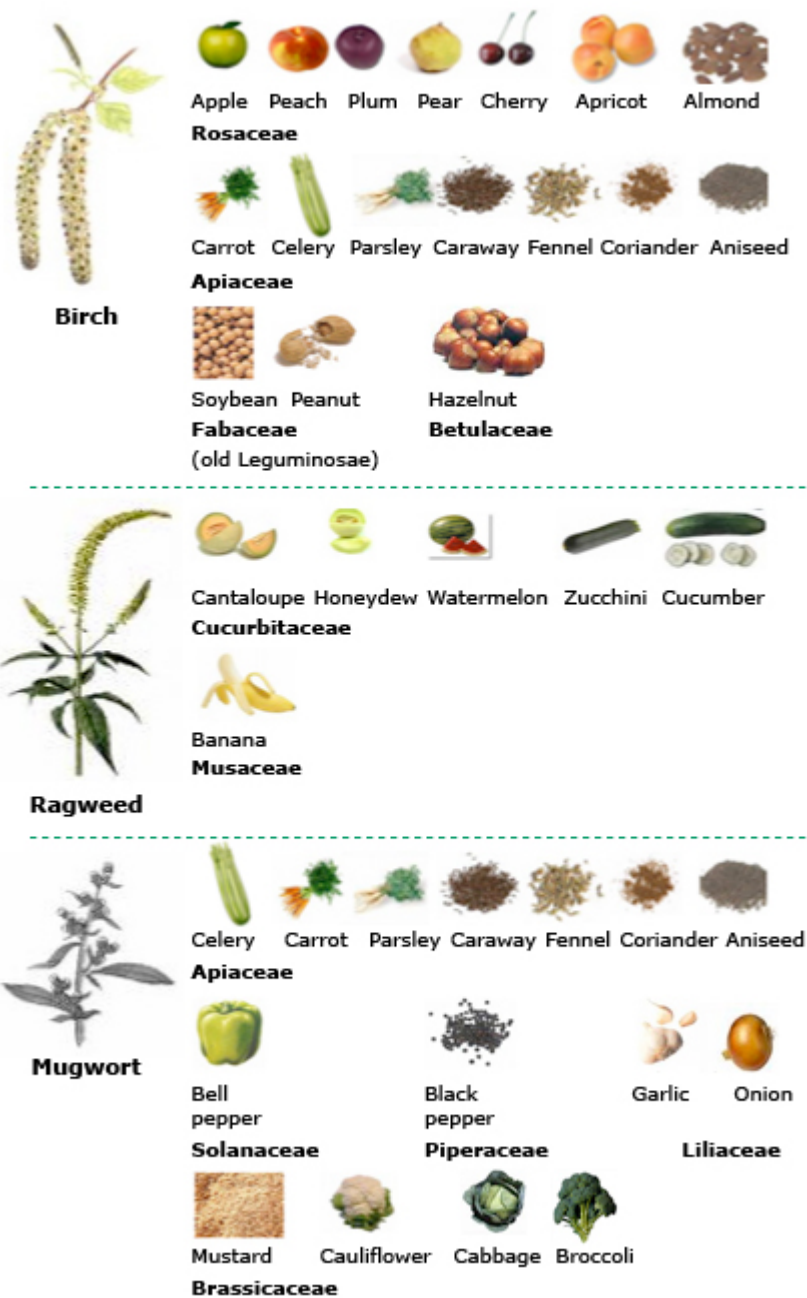
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GRAPHICS

Cross-reactivity patterns in pollen-food allergy syndrome



Typical patterns of cross-reactivity between pollens and fruits and vegetables. Individual foods are grouped by their taxonomical families. *Adapted and extended from: Sicherer, SH. Clinical implications of cross-reactive food allergens.*

J Allergy Clin Immunol 2001; 108:881.

Peak pollen periods in the United States

	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
Northeast				Trees		Grasses			Weeds			
Mid-Atlantic			Trees		Grasses			Weeds				
Southeast		Trees			Grasses			Trees				
Midwest		Trees			Grasses			Weeds				
Northwest		Trees			Grasses			Weeds				
Southwest		Trees			Grasses			Weeds				
